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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,383	FLOEGE ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 22-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 22-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-7 and 22-33 are pending.

2. Applicant's election without traverse of Group I, claims 1-7 (now claims 1-7 and 22-33) drawn to a method of treating nephritis using antibody that binding to platelet derived growth factor-DD (PDGF-DD), filed 2/15/01, is acknowledged.

3. Claims 1-7 and 22-33, drawn to a method of treating nephritis using antibody that binding to platelet derived growth factor-DD (PDGF-DD), are being acted upon in this Office Action.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-7 and 22-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a method of treating mesangial cell proliferative nephritis or glomerulonephritis comprising selecting an animal in need of treatment for nephritis, and administering to the animal a therapeutic effective dose of a neutralizing antibody mAb 6.4 or binding fragment thereof that binds specifically to either mouse or human platelet factor-DD (PDGF-DD) wherein said neutralizing antibody or binding fragment thereof neutralizes PDGF-DD induced mitogenic activity of mesangial cell, (2) the said method wherein said neutralized antibody is a human antibody, or a fully human monoclonal antibody, (3) the said method wherein the neutralized antibody has a Kd in the range of about 10^{-6} to 10^{-11} M as measured in either solid phase or solution phase, (4), the said method wherein said neutralized antibody comprises a fully human IgG2 heavy chain and a human kappa light chain, and (5) the said method wherein said neutralized antibody is administered via subcutaneous or intramuscular injection, **does not** reasonably provide enablement for a method of treating any nephritis, any nephritis such as mesangiocapillary glomerulonephritis, systemic lupus erythematosus, progressive renal disease, any renal interstitial fibrosis, any renal failure and any diabetic nephropathy by administering any neutralizing antibody or binding fragment thereof that neutralizes any PDGF-DD induced mitogenic activity, any neutralizing antibody or binding

fragment thereof that "cross-reacts" with fully human anti-PDGF-DD antibody mAb6.4 or any antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 as set forth in claims 1-7 and 22-33. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The claims encompass a method of treating any nephritis by administering any anti-PDGD-DD that cross-react with fully human anti-PDGF-DD antibody mAb 6.4 or any antibody in the same "antigen-binding bin" as fully human anti-PDGF-DD antibody mAb 6.4.

The term "nephritis" as defined in the specification at page 6 [paragraph 0016] is any disease or condition or can be nephritis and related diseases, including but *not limited to*, nephritis, progressive renal diseases, and related diseases, such as mesangial proliferative nephritis, mesangial proliferative glomerulonephritis, mesangiocapillary glomerulonephritis, systemic lupus erythematosus, glomerular nephritis, renal interstital fibrosis, renal failure, and diabetic nephropathy. The anti-PDGF-DD antibodies may be administered *to prevent* a mammal from contracting diseases or conditions associated with the expression of PDGF-DD including, but not limited to, nephritis or related diseases, and diseases caused by mesangial proliferation. Preferably the anti-PDGF-DD antibodies are fully human.

The specification discloses only a method of treating mesangial cell proliferative nephritis or glomerulonephritis by administering only neutralizing anti-PDGF-DD mAb 6.4 or binding fragment thereof to Male Wistar rats with anti-Thy-1 induced nephritis. The male Wistar rats induced with anti-Thy-1 are a model for acute human mesangial cell proliferative nephritis or glomerulonephritis. The neutralizing antibody or binding fragment thereof neutralizes PDGF-DD induced mitogenic activity of mesangial cell (see Figure 12).

The specification does not teach how to treat any nephritis disorder as defined above such as mesangiocapillary glomerulonephritis, systemic lupus erythematosus, progressive renal disease, any renal interstitial fibrosis, any renal failure and any diabetic nephropathy by administering to the animal any anti-PDGF-DD antibody or binding fragment thereof, or any anti-PDGF-DD antibody or binding fragment that cross react with mAb 6.4 or in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4.

The male Wistar rats induced with anti-Thy-1 are only an experimental model for *acute* human mesangial cell proliferative nephritis or glomerulonephritis. However, male Wistar rats induced with anti-Thy-1 is not a model for any other autoimmune diseases, any autoimmune disease such as Systemic lupus erythematosus.

Van Noort *et al* teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). It is not clear the reliance of male Wistar rats induced with anti-Thy-1 is the appropriate model for any and all autoimmune disease.

With respect to capillary glomerulonephritis (endothelial cell proliferative glomerulonephritis), Iruela-Arispe et al teach anti-PDGF antibody treatment of glomerulonephritis has no effect on endothelial cells proliferation and capillary repair (see abstract, page 1722, paragraph bridging col. 1 and 2, Table 2, in particular).

Further, there is no guidance as how to "prevent" any nephritis mentioned above by administering any anti-PDGF-DD antibody. The term "prevent" as define by the Webster's II New Riverside University Dictionary as "to keep from happening or to anticipate or counter in advance". There is a lack of in vivo working example as how to select or identify an individual who may or may not have any nephritis, any progressive renal disease, any renal interstitial fibrosis, any renal failure, any diabetic nephropathy or any autoimmune disease such as systemic lupus erythematosus, much less for preventing such diseases from happening in those individual.

The specification does not teach anti-PDGF-DD antibody amino acids cross-react with the fully human anti-PDGF-DD antibody mAb 6.4. The specification does not teach the "antigen-binding bin" of fully human anti-PDGF-DD antibody mAb6.4 without the amino acid sequence. The specification does not teach any assays that is useful for screening variants of anti-PDGF-DD and is predictive of success in preventing any disease in vivo. It is known in the art that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site of antibody can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the unlimited number of undisclosed anti-PDGF-DD antibody for treating and preventing any nephritis mentioned above, the actual biological activity of such antibodies remain to be demonstrated in mesangial proliferative glomerulonephritis, let alone the claimed method could prevent any nephritis as broadly as defined in the specification.

Given the unlimited of diseases and unlimited number of anti-PDGF-DD antibody, it is unpredictable which undisclosed anti-PDGF-DD antibody would be useful for treating, including preventing any and all diseases.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

6. Claims 1-7 and 22-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of any anti-PDGF-DD or binding fragment thereof that "cross-reacts" with fully human anti-PDGF-DD antibody mAb 6.4 or any anti-PDGF-DD or binding fragment thereof in the same "antigen-binding bin" as fully human anti-PDGF-DD antibody mAb 6.4 that is effective in treating any nephritis.

The term "nephritis" as defined in the specification at page 6 [paragraph 0016] is any disease or condition or can be nephritis and related diseases, including but *not limited to*, nephritis, progressive renal diseases, and related diseases, such as mesangial proliferative nephritis, mesangial proliferative glomerulonephritis, mesangiocapillary glomerulonephritis, systemic lupus erythematosus, glomerular nephritis, renal interstital fibrosis, renal failure, and

diabetic nephropathy. The anti-PDGF-DD antibodies may be administered *to prevent* a mammal from contracting diseases or conditions associated with the expression of PDGF-DD including, but not limited to, nephritis or related diseases, and diseases caused by mesangial proliferation. Preferably the anti-PDGF-DD antibodies are fully human.

The specification discloses only a method of treating mesangial cell proliferative nephritis or glomerulonephritis by administering only neutralizing anti-PDGF-DD mAb 6.4 or binding fragment thereof to Male Wistar rats with anti-Thy-l induced nephritis. The male Wistar rats induced with anti-Thy-1 are a model for acute human mesangial cell proliferative nephritis or glomerulonephritis. The neutralizing antibody or binding fragment thereof neutralizes PDGF-DD induced mitogenic activity of mesangial cell (see Figure 12).

With the exception of the specific neutralizing anti-PDGF-DD mAb 6.4 or binding fragment thereof for treating only mesangial cell proliferative nephritis or glomerulonephritis, there is insufficient written description about the structure associated with function such as binding specificity of any and all other anti-PDGF-DD antibody or binding fragment thereof that "cross-reacts" with anti-PDGF-DD mAb 6.4.

Given the unlimited number of nephritis diseases or conditions as defined by the specification, there is inadequate written description about the method of treating, including "preventing" other diseases such as systemic lupus erythematosus, glomerular nephritis, renal interstital fibrosis, renal failure, and diabetic nephropathy by administering any anti-PDGF-DD or binding fragment thereof.

The specification discloses only one anti-PDGF-DD mAb 6.4 that is useful for treating only mesangial cell proliferative nephritis or glomerulonephritis by inhibiting mesagial cell proliferation, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of anti-PDGF-DD antibody and diseases to describe the genus for the claimed method. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "antigen-binding bin" in claim 1 is ambiguous and indefinite because one of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-2, 4-5 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (J. Exp Med 175: 1413-1416, May 1992; PTO 892).

Johnson et al teach a method of treating nephritis such as mesangial cells proliferative glomerrulonephritis by administering via injection to the animal such as Wistar rats induced anti-Thy-1 (a model for human mesangial cells proliferative glomerrulonephritis) a neutralizing polyclonal antibody that binds to and neutralized all dimeric forms of human PDGF (see entire document, abstract, page 1413, col. 2, anti-PDGF antibody, in particular). The reference anti-PDGF antibody inherently cross-reacts with the claimed fully human anti-PDGFDD antibody mAb 6.4 because the reference antibody inhibits mesangial cell proliferation (mitogenic activity) (See page 1414, col. 2, Table 1, and inhibits extracellular matrix accumulation (see page 1415, Table 2, in particular) in the same glomerular nephritis model used by applicant (see Materials and Methods, in particular). The reference antibody appears to be in the same antibody-binding bin as the fully human anti-PDGF-DD antibody since it inhibits mesangial cell proliferation (mitogenic activity) (See page 1414, col. 2, Table 1, and inhibits extracellular matrix accumulation (see page 1415, Table 2, in particular). The reference antibody inherently has a Kd in the range of about 10^{-6}M. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195

USPQ 430(CCPA 1977). Claim 2 is included in this rejection because the reference method is intended for treating human since the reference model is a human model of mesangial cells proliferative glomerrulonephritis. Thus, the reference teachings anticipate the claimed invention.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 3 and 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (J. Exp Med 175: 1413-1416, May 1992; PTO 892) in view of LaRochelle et al (Nature Cell Biology 3: 517-521, May 2001; PTO 892) and WO 96/34096 (Oct 1996; PTO 892) or US Pat No. 6,207,418 (March 27, 2001; PTO 892).

The teachings of Johnson et al have been discussed supra.

The invention in claims 3 and 28 differs from the teachings of the reference only in that the method of treating nephritis wherein the anti-PDGF-DD antibody is fully human monoclonal antibody.

The invention in claims 23 and 25 differs from the teachings of the reference only in that the method of treating nephritis wherein the antibody comprises a fully human IgG2 heavy chain.

The invention in claims 24 and 26 differs from the teachings of the reference only in that the method of treating nephritis wherein the antibody comprises a fully human IgG2 heavy chain and a human kappa light chain.

LaRochelle et al teach various PDGF-DD such as human and mouse PDGF-DD sequence that have a long stretch of identical amino acids to PDGF-C, PDGF-B and PDGF-A (see sequence alignment on page 518, Fig 1b, page 517, col. 1, in particular). LaRochelle et al teach PDGF-D is expressed in kidney and forms dimer such as PDGF-DD (see page 517, col. 2, last paragraph, in particular). LaRochelle et al teach PDGF-DD may play a role in human diseases such as trauma, fibrotic disease or malignancy and targeting PDGF-DD's growth-promoting properties is useful for therapeutic purposes (see page 520, col. 1, in particular).

The WO 96/34096 publication teaches a method of producing human antibody and binding fragment thereof such as F(ab)2 to any human antigen such as growth factor from the PDGF family for treatment of glomerular nephritis (See entire document, page 13, lines 33-35, page 37, lines 26-28, page 31, claims 1-5, 18 and 45, of WO 96/34096 publication, in particular). The WO 96/34096 publication teaches the advantage human antibody is that it is less immunogenic since it is a fully human antibody (See page 1, lines 28-35, in particular).

The '418 patent teaches a method of making human antibody to any antigen having the desirable human kappa light chain and human IgG2 heavy chain for treatment of autoimmune disease (see entire document, col. 3, lines 3-13, claims 1-11 of the '418 patent, in particular). The '418 patent teaches the advantage of IgG2 heavy chain is that it blocks the binding of a ligand to a receptor and not cause cell killing (see col. 3, lines 10-14, in particular). The reference human antibody binds with high affinity and can be measure in solution phase (see col. 3, line 14, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make any fully human antibody that binds to any antigen of interest as taught by the WO 96/34096 publication or the '418 patent having a human IgG2 heavy chain using the human or mouse PDGF-DD as taught by LaRochelle et al for a method of treating nephritis as taught by Johnson et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because fully human antibody is less immunogenic as taught by the WO 96/34096 publication (See page 1, lines 28-35, in particular). The '418 patent teaches the advantage of fully human antibody having IgG2 heavy chain is that it blocks the binding of a ligand to a receptor and not cause cell killing (see col. 3, lines 10-14, in particular). Johnson et al teach anti-PDGF dimer is useful for treating

nephritis such as mesangial cells proliferative glomerrulonephritis. LaRochelle et al teach PDGF-DD may play a role in human diseases such as trauma, fibrotic disease or malignancy and targeting PDGF-DD's growth-promoting properties is useful for therapeutic purposes (see page 520, col. 1, in particular).

14. Claims 1 and 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (J. Exp Med 175: 1413-1416, May 1992; PTO 892) in view of US Pat No US Pat 6,706,687 B1 (filed 11/1999; PTO 892).

The teachings of Johnson et al have been discussed supra.

The invention in claim 6 differs from the teachings of the reference only in that the method of treating nephritis wherein the administration is via subcutaneous injection.

The invention in claim 7 differs from the teachings of the reference only in that the method of treating nephritis wherein the administration is via intramuscular injection.

The '687 patent teaches a method of inhibiting PDGF-D mediated conditions such as proliferation of tumor cells, angiogenesis, lymphangionesis by administering monoclonal, chimeric or humanized monoclonal antibody that binds specifically to PDGF-D dimer (see col. 9, lines 50, col. 10, lines 51-67, col. 11, lines 1-7, in particular). The route administration such as subcutaneous or muscular injection is within the purview of one ordinary skill-attending physician or veterinarian (see col. 13, lines 4-10, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer anti-PDGF-DD antibody for treatment of nephritis as taught by Johnson et al via subcutaneous or muscular injection as taught by the '687 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because it is within the purview of one ordinary skill in the pharmaceutical art to administering any PDGF-D inhibitor via subcutaneous or muscular injection as taught by the '687 patent (see col. 13, lines 4-11, in particular). Johnson et al teach anti-PDGF dimer is useful for treating nephritis such as mesangial cells proliferative glomerrulonephritis.

15. Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (J. Exp Med 175: 1413-1416, May 1992; PTO 892) in view of LaRochelle et al (Nature Cell Biology 3: 517-521, May 2001; PTO 892), and WO 96/34096 publication (Oct 1996; PTO 892) or US Pat No. 6,207,418 (March 27, 2001; PTO 892) as applied to claims 1, 3 and 23-30 mentioned above and further in view of US Pat No US Pat 6,706,687 B1 (filed 11/1999; PTO 892).

The combined teachings of Johnson et al, LaRochelle et al, and WO 96/34096 publication or the '418 patent have been discussed supra.

The invention in claim 31 differs from the combined teachings of the references only in that the method of treating nephritis wherein the administration is via subcutaneous injection.

The invention in claim 32 differs from the combined teachings of the references only in that the method of treating nephritis wherein the administration is via intramuscular injection.

The '687 patent teaches a method of inhibiting PDGF-D mediated conditions such as proliferation of tumor cells, angiogenesis, lymphangiogenesis by administering monoclonal, chimeric or humanized monoclonal antibody that binds specifically to PDGF-D dimer (see col. 9, lines 50, col. 10, lines 51-67, col. 11, lines 1-7, in particular). The route administration such as subcutaneous or muscular injection is within the purview of one ordinary skill-attending physician or veterinarian (see col. 13, lines 4-10, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administering fully human anti-PDGF-DD antibody comprising human IgG2 heavy chain and human kappa light chain as taught by the LaRochelle et al, and WO 96/34096 publication or the '418 patent for treatment of nephritis as taught by Johnson et al via subcutaneous or muscular injection as taught by the '687 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because it is within the purview of one ordinary skill in the pharmaceutical art to administering any PDGF-D inhibitor via subcutaneous or muscular injection as taught by the '687 patent (see col. 13, lines 4-11, in particular).

16. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (J. Exp Med 175: 1413-1416, May 1992; PTO 892) in view of LaRochelle et al (Nature Cell Biology 3: 517-521, May 2001; PTO 892), and WO 96/34096 publication (Oct 1996; PTO 892) or US Pat No.

6,207,418 (March 27, 2001; PTO 892) as applied to claims 1, 3 and 23-30 mentioned above and further in view of US Pat No. 6,630,142 (filed May 3,1999; PTO 892).

The combined teachings of Johnson et al, LaRochelle et al, and the WO 96/34096 publication or the '418 patent have been discussed supra.

The invention in claim 33 differs from the combined teachings of the references only in that the method of treating nephritis wherein the antibody has a kD in the range of about 10^{-6} M measured in either solid phase or solution phase.

The '142 patent teaches the binding affinity of an antibody can be readily determined by one of ordinary skill in the art, for example, by Scatchard analysis, Methods for screening and isolating specific antibodies are well known in the art (see col. 14, lines 13-23, in particular). The binding affinity should be at least 10 fold greater than the binding affinity of control antibody (see col. 14, lines 4-8, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the antibody binding affinity (Kd) by Scatchard analysis as taught by the '142 patent using the fully human antibody that binds specifically to PDGF-DD comprising human IgG2 heavy chain and human kappa light chain as taught by the LaRochelle et al, WO 96/34096 publication and the '418 patent with the expectation that the binding affinity or kD in the range of at least about 10^{-6} M for a method of treating nephritis as taught by Johnson et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the binding affinity of an antibody can be readily determined by one of ordinary skill in the art using Scatchard analysis that is done in solid phase or solution phase as taught by the '142 patent. The recitation of Kd in the range of about 10^{-6} M (low affinity) to 10^{-11} M (high affinity) is within the purview of one ordinary skill in the art since the binding affinity should be at least 10 fold greater than the binding affinity of control antibody as taught by the '142 patent (see col. 14, lines 4-8, in particular).

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The

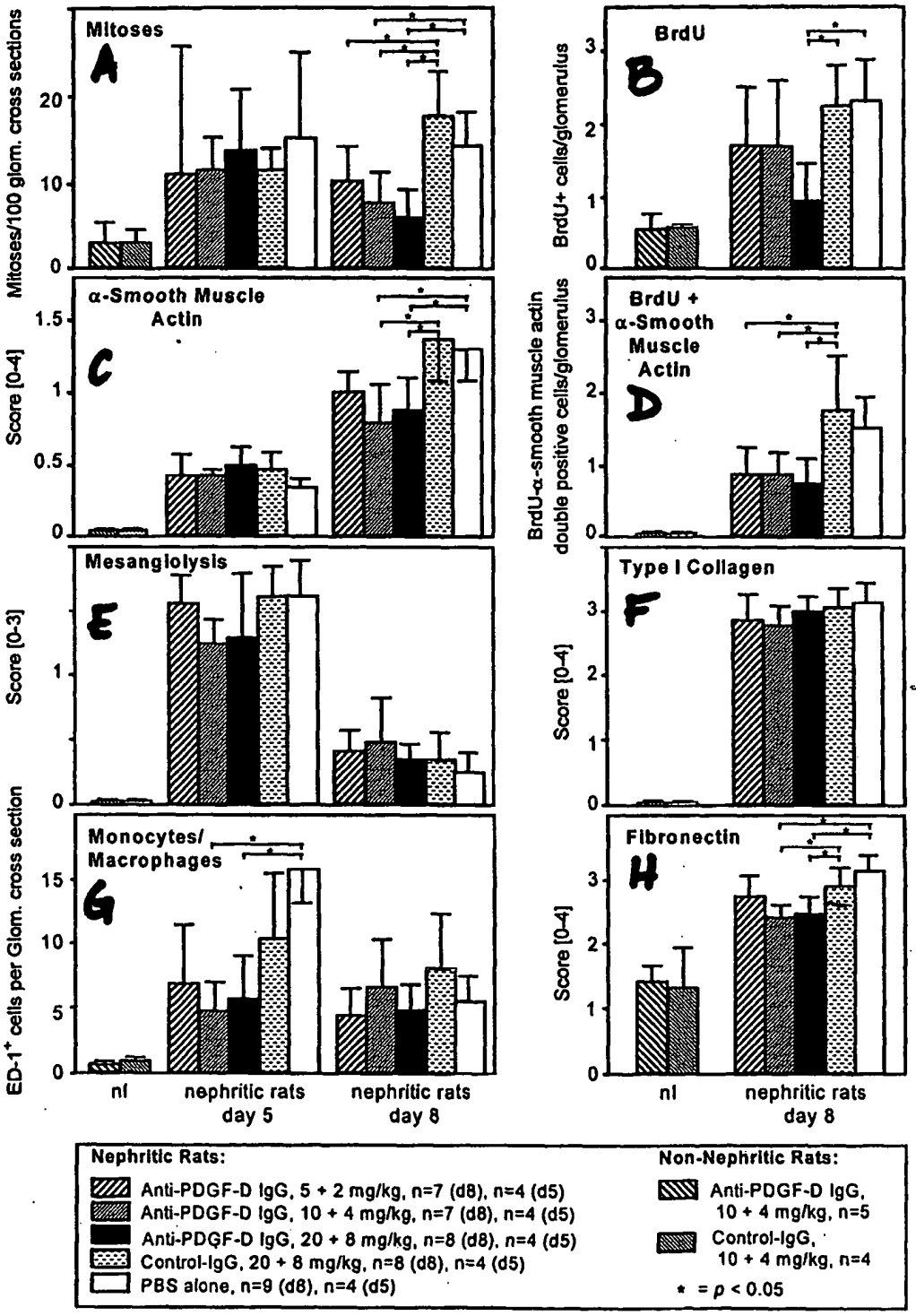
examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

19. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
February 17, 2006

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

FIGURE 12


Mitoses
A
Mitoses/100 glom. cross sections
BrdU
B
BrdU+ cells/glomerulus
α-Smooth Muscle Actin
C
Score [0-4]
BrdU + α-Smooth Muscle Actin
D
BrdU-α-smooth muscle actin double positive cells/glomerulus
Mesangiolysis
E
Score [0-3]
Type I Collagen
F
Score [0-4]
Monocytes/ Macrophages
G
ED-1+ cells per Glom. cross section
Fibronectin
H
Score [0-4]
nl
nephritic rats day 5
nephritic rats day 8
nl
nephritic rats day 8
Nephritic Rats:
Anti-PDGF-D IgG, 5 + 2 mg/kg, n=7 (d8), n=4 (d5)
Anti-PDGF-D IgG, 10 + 4 mg/kg, n=7 (d8), n=4 (d5)
Anti-PDGF-D IgG, 20 + 8 mg/kg, n=8 (d8), n=4 (d5)
Control-IgG, 20 + 8 mg/kg, n=8 (d8), n=4 (d5)
PBS alone, n=9 (d8), n=4 (d5)
Non-Nephritic Rats:
Anti-PDGF-D IgG, 10 + 4 mg/kg, n=5
Control-IgG, 10 + 4 mg/kg, n=4
* = p < 0.05